concomitant radiochemotherapy in patients affected by head and neck cancer.

Material and Methods: 226 patients, 38 female and 188 male, with head and neck cancer, treated with chemoradiotherapy from 1995 to 2014 at our department, were retrospectively reviewed. 59,7% of patients were younger than 60 years. The anatomical sites of cancer were: 36 nasopharynx, 63 oropharynx, 34 oral cavity, 51 larynx, 26 hypopharynx, 16 others sites. 64 patients underwent to post-operative treatment and 162 to radical treatment. They were treated with 2D-3DCRT (80%) or IMRT technique (20%). The mean dose administered was 68 Gy (range 60-74). The schedule of chemotherapy most used included cisplatin and 5-FU. Acute and late toxicity are assessed according to CTCAE v.4.0 scale. Age, gender, tumor/nodal stage, primary site, tumor grading, RT technique and dose were assessed as potential prognostic factors influencing treatment toxicity.

Results: Acute dysphagia and mucositis G2-3 were observed in 82,7% and 84,9% respectively of patients and were related with young age (p=0,03 and p=0,02), pharynx site (p=0,004 and p<0,003) and advanced stage (p=0,02 and p=0,009). Acute xerostomia G2-3 (15%) was associated with oropharyngeal and oral cavity sites (p=0,03) and RT technique (p=0,004). Late xerostomia G2-3 (25,2%) was related with oropharyngeal site (p=0,04) and late fibrosis (14,1%) with nodal stage (p=0,005). Acute and late hearing loss (4,8%) was observed more frequently in nasopharyngeal cancer (p=0,03 and p=0,001 respectively). 3,5% of patients had acute neurotoxicity and 4,8% late neurotoxicity; this adverse effect was associated with nasopharyngeal site (p=0,03 and p=0,03 respectively).

		Gender	Age	Pharynx site	Stage	Nodal stage	Grading	Dose	RT technique
dysphagia	acute	p=0,6	p=0,03	p=0,004	p=0,02	p=0,9	p=0,6	p=0,1	p=0,9
	late	p=0,1	p=0,8	p=0,3	p=0,9	p=0,9	p=0,4	p=0,1	p=0,6
mucositis	acute	p=0,6	p=0,02	p<0,003	p=0,009	p=0,2	p=0,1	p=0,1	p=0,9
xerostomia	acute	p=0,6	p=0,9	p=0,03	p=0,08	p=0,04	p=0,08	p=0,7	p=0,004
	late	p=0,1	p=0,2	p=0,04	p=0,9	p=0,6	p=0,7	p=0,6	p=0,5
neurotoxicity	acute	p=0,8	p=0,8	p=0,03	p=0,4	p=0,09	p=0,7	p=0,4	p=0,7
	late	p=0,7	p=1	p=0,03	p=0,7	p=0,5	p=0,01	p=0,1	p=0,8
hearing loss	acute	p=1	p=0,5	p=0,03	p=0,7	p=0,5	p=0,6	p=0,8	p=0,5
	late	p=1	p=0,2	p=0,001	p=0,1	p=0,5	p=0,6	p=0,5	p=0,8
fibrosis	late	p=0,9	p=0,8	p=0,6	p=0,3	p=0,005	p=0,2	p=0,6	p=0,2

Conclusion: Clinical and technical data may be predictive of severe toxicity. Younger patients with pharynx cancer are more susceptible to dysphagia, mucositis and xerostomia. In this subset of patients it's critical evaluate strategies of adaptive radiotherapy with the aim to decrease the toxicity.

EP-1078

Nasopharyngeal Carcinoma: prognostic factors analysis in patients treated with IMRT and chemotherapy

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Purpose or Objective: To analyze clinical outcome and prognostic factors in a consecutive series of 160 non-metastatic nasopharyngeal carcinoma (NPC) patients (pts) treated curatively with intensity modulated radiotherapy (RT) techniques (IMRT, Intensity Modulated Radiation Therapy or VMAT, Volumetric Modulated Arc Therapy) and chemotherapy (CT).

Material and Methods: Pts were treated between October 2004 and April 2014 at our institution. Median age at diagnosis was 49 years (range 18-92). According to WHO, 144 patients (90%) were suffering from undifferentiated NPC, 5 patients (3.1%), 3 patients (1.9%) and 8 patients (5%) were respectively affected by squamous cell carcinoma G1, G2 or G3. One pt was in stage I (0.6%), 31 pts (19.4%) were in stage II, 47 pts (29.4%) in stage III, 31 pts (19.4%) in stage IVA and 50 pts (31.2%) in stage IVB. Seven pts (4.4%) received RT alone: 1 pt in stage I and 6 pts in stage II. Of the remaining 153 pts (95.6%) (25 pts with stage II and 128 pts with stage III and IV) 34 patients (21.2%) received CT concomitant to RT and 119 patients (74.4%) were treated with induction CT followed by RT-CT. IMRT was given with standard fractionation at a total dose of 70 Gy. In 134 patients (83.75%) circulating plasma EBV-DNA has been measured before treatment using quantitative PCR. A dedicated software (VODCA, www.vodca.ch) was used to collect and analyze dosimetric parameters in 137 pts.

Results: With a median follow up of 55.7 months (range 3.8 - 118.7) actuarial rates at 2 and 5 years were respectively: overall survival (OS) 92.36% and 82.81%, disease-free survival (DFS) 83.1% and 77.2%, local control (LC) 92.17% and 90.43%, locoregional control (LRC) 94.78% and 93.04% and distant control (DC) 89.57% and 86.96%. At univariate analysis N stage (N0+N1+N2+N3a vs N3b) was found to be a prognostic factor for DM (p = 0.029). At multivariate analysis conducted on the following parameters: T stage, N stage, stage, RT technique , V95%, Dmean and D99% (relative to High Risk PTV), the stage of T (T1+T2+T3 vs T4) was found to be a prognostic factor for LRC (p = 0.035). Both at univariate and multivariate analysis the stage of T was found to be a prognostic factor for LC (p = 0.004 and .011 respectively) and N stage (N0+N1+N2 vs N3) for DM and RC. Pts with a V95% > 90% had better LC (p=0.004) and DFS (p=0.047). Pts with a Dmean > 69 Gy had better LC (p=0.029). Pts with a D99% > 64 Gy had better LC (p=0.008) and OS (p=0.004). The threshold value of 45 cc of GTV T (Gross Tumor Volume of the primary tumor) was prognostic for LC (p = 0.0095). The threshold value of 1500 copies of EBV-DNA was prognostic for DC (p = 0.048).

Conclusion: The intensified treatment of CT-IMRT / VMAT achieves excellent clinical outcomes. Besides traditional prognostic factors, we demonstrated the prognostic value of dosimetric parameters. Finally, for the first time in a non-endemic area threshold values of GTV T and EBV-DNA prognostic for LC and DC respectively have been confirmed.

EP-1079

Clinical outcomes in locally advanced oropharyngeal cancer 18FDG PET-guided dose escalation IMRT-SIB

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Purpose or Objective: Technological advances have enabled clinicians to explore dose escalation strategies in various tumor sites. Intermediate and high risk oropharyngeal cancers have unsatisfactory 3 year outcomes. The simultaneous integrated boost (SIB) technique with dose per fraction slightly higher than 2Gy offers the advantages of shortening the treatment time and increasing the biologically equivalent dose to the tumor. This retrospective study is aimed to evaluate the clinical outcome of radiation dose escalation to 18FDG PET/CT positive tumor and nodal sub volumes using the Simultaneous Integrated Boost (SIB) IMRT technique by means of Helical Tomotherapy (HT) in locally advanced Oropharyngeal cancer patients (pts).

Material and Methods: 37 pts, median age 59 years (range: 41-81), treated between 2005 and 2014, were evaluated. Reported stage were III-IVAB (4 and 33 respectively). HT was delivered with the SIB technique at different dose levels: 69Gy (2.3 Gy/day) to the PET-positive volume (GTV-PET), 66

Gy (2.2 Gy/day) to the clinical target volume for tumor and metastatic nodal station, 54 Gy (1.8 Gy/day) to the clinical negative neck region concomitantly in 30 fractions. Concurrent chemotherapy was given to 32 pts (cisplatin 75-100 mg/m²/21 days for 25 pts, cisplatin 30-40 mg/m²/week for 5 pts and Cetuximab for 2). Possible correlation between Overall Cancer specific (OS) and GTV-PET Volumes (GTV-T+N, GTV-T, GTV-N) was also considered.

Results: The median follow-up was 39.2 months (range: 3-125); 27%, 62% and 11% pts has respectively never smoked, a smoking history of more than 10 packs/year and not assessed. 36 pts completed the treatment as scheduled. Temporary treatment interruption due to acute toxicity, mainly mucosae, was observed in 5 patients. No grade 4 acute mucosae and skin toxicity was reported. Seventeen pts (46%) experienced grade 3 toxicity, mostly dermatitis and mucositis. Late grade 3 and 2 xerostomia was seen respectively in 3% and 32% pts. No grade 4 late toxicity was observed. The 3-year OS, Local disease-free Tumor (LTC), Local disease-free Nodal (LNC) and distant metastasis-free (DMFS) survivals were 87%, 83%, 89% and 92% respectively. Multivariate Cox regression analyses revealed that GTV-T+N and GTV-T are predictors for OS with a best-cut-off value equal to 30.9 cc (p=0.005) and 22.4 cc (p=0.038).

Conclusion: The slightly accelerated dose escalation in oropharyngeal cancers to 18FDG-PET positive tumour sub-volumes is likely to be safe even with concurrent chemotherapy. Very interesting 3-year OS and loco-regional disease control rate are obtained. The results of the present study suggest that GTV-PET has a predictive value for the SIB-HT outcome. These findings may constitute the basis for more personalized treatments.

EP-1080

Definitive or adjuvant IMRT for locally advanced sinonasal tumors: outcome and prognostic factors

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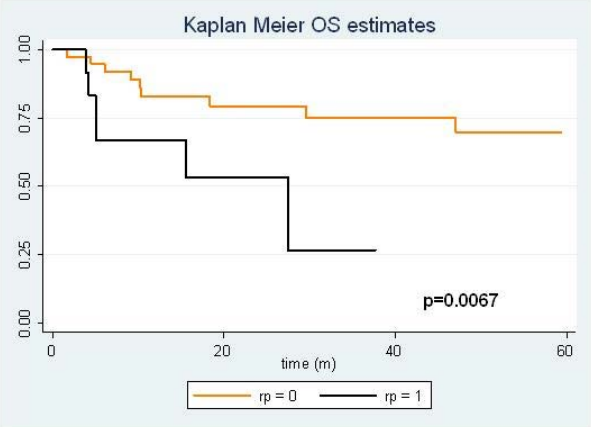
Purpose or Objective: There are limited and heterogeneous data on prognostic factors of locally advanced epithelial non glandular sinonasal cancer (ESNC) treated with multimodal treatment strategy. Prognosis of ESNC remains poor, with an overall 5-year survival rate of 30–50%. We analyzed a retrospective series of consecutive patients (pts) treated with IMRT at our institution, with a specific focus on the prognostic implications of clinical and treatment-related factors.

Material and Methods: Since 2007, 49 pts with ESNC staged III and IVA-IVB were treated at our Institution. Histology was squamous cell carcinoma (SCC) in 22 pts (44.9%), undifferentiated carcinoma (SNUC) in 20 pts (40.8%) and neuroendocrine carcinoma (SNEC) in 7 pts (14.3%). Prevalent primary site was ethmoid sinus (24 pts, 49%). Thirteen pts (26.5%) had N stage≥2b and 12 (24.5%) had positive retropharyngeal nodes (RPNs). Orbital apex invasion (OAI), nasopharyngeal involvement, gross nerves involvement (GNI) and positive surgical margins (R1) were found in 24 (49%), 12 (24.5%), 10 (20.4%) and 5 (10.2%) pts respectively. Thirty (61.2%) and 19 (38.8%) pts received definitive and postoperative IMRT, respectively. Thirtyfive pts (71.5%) received induction chemotherapy before surgery or RT and/or concomitant CHT. Thirtyeight pts (77.5%) received concomitant CHT. IMRT was given with standard fractionation at a total dose of 65-72 Gy in definitive cases and 54-66 Gy in adjuvant cases, according to histological findings. Gross tumor volume (GTV) was defined in all radical pts, and dose-volume histograms to all targets were analyzed in all pts.

Results: Median follow up was 22.4 months (range 6-85). Three-year overall survival (OS), disease free survival (DFS) and locoregional control (LRC) were respectively 66.5%, 55.4% and 66.3% for the entire cohort. OS and DFS were statistically better in pts with SCC or SNUC compared to pts with SNEC, in pts with ethmoid primary compared to other sites, in pts with N0 compared to pts with N stage ≥ 2b, in pts with RPNs compared to pts without RPNs (see Fig. 1), in pts with OAI compared to pts without OAI and in pts with GNI compared to pts without GNI. LRC was better even though statistically not different in pts without R1 compared to pts with R1. A multivariate analysis showed that ethmoid as primary origin site was a positive independent prognostic factor on OS, whereas RPNs positivity and OAI were negative independent prognostic factors for OS. For pts receiving definitive IMRT, pts with GTV <79.7cc had better OS, DFS and LRC compared to pts ≥79.7 cc, even if the difference was not statistically significant. Dosimetric factors were not found to have any prognostic role.



Conclusion: In a monoinstitutional series of locally advanced ESNC we obtained a 66.5% 3-yr OS and a 55.4% 3-yr DFS. We were able to identify RPNs involvement, ethmoid primary site and OAI as independent prognostic factors.

EP-1081

Advanced head and neck ca - chemoradiotherapy with conventional fraction and accelerated fraction

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Purpose or Objective: To compare early tumor response and compliance of locally advanced head and neck cancer patients receiving concurrent chemo-radiation, weekly Cisplatin with conventional fractionation versus weekly Cisplatin with accelerated fractionation and to assess toxicity profile

Material and Methods: Patients with histologically confirmed primary head and neck squamous cell carcinoma, stage III and IV (Oral cavity, oropharynx, hypopharynx and larynx) attending the department of Radiotherapy, Father Muller Medical College Hospital, Mangalore Between November 2013 to April 2015.
Total of 64 patients were recruited and randomized into conventional and accelerated arm each having 32 patients.